Determination of the Normal Range for Thyroid Uptake of Technetium-99m Pertechnetate in a Turkish population

Türk Bir Popülasyonda Normal Tiroid Teknesyum-99m Perteknetat Alım Aralığının Belirlenmesi

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Abstract

Aim: This study aimed to determine the normal range for thyroid uptake of technetium-99m (^{99m}Tc) pertechnetate in a Turkish population.

Methods: The retrospective study included 73 (54 females, 19 males) consecutive euthyroid patients, all of whom underwent thyroid scintigraphy using ^{99m}Tc-pertechnetate as a component of parathyroid scintigraphy for parathyroid adenoma localization. The value of thyroid uptake of ^{99m}Tc-pertechnetate at the 20th minute was calculated for each patient.

Results: The mean patient age was 56.4±15.2 years; the mean thyroid-stimulating hormone level was 1.15±0.48 uIU/mL. The median and interquartile range values of 99mTc-pertechnetate uptake were 0.8% and 0.56–1.15%, respectively. The normal range for thyroid uptake of 99mTc-pertechnetate was determined to be 0.26–1.64%. There was a negative correlation between 99mTc-pertechnetate uptake and age (r =-0.33, p=0.002).

Conclusion: We propose that our new normal range for thyroid uptake of ^{99m}Tc-pertechnetate based on significantly lower values compared with those currently in use in Turkey is appropriate for use to evaluate thyroid function in thyroid disorders in the population of Istanbul.

Keywords: technetium-99m pertechnetate; thyroid; thyroid scintigraphy

Öz

Amaç: Bu çalışmada Türk bir popülasyonda normal tiroid teknesyum-99m perteknetat alım aralığını belirlemek amaçlanmıştır.

Yöntem: Retrospektif çalışmamız paratiroid adenom lokalizasyonu için uygulanan paratiroid sintigrafisinin bir bileşeni olarak teknesyum-99m perteknetat ile tiroid sintigrafisi yapılan ardışık 73 (54 kadın, 19 erkek) ötiroid hasta içerdi. Her hasta için 20. dakikada tiroid teknesyum-99m perteknetat alım değeri hesaplandı.

Bulgular: Ortalama hasta yaşı 56,4±15,2 yıl, ortalama tiroid uyarıcı hormon düzeyi 1,15±0,48 uIU/mL idi. Medyan ve çeyrekler arası aralık teknesyum-99m perteknetat alım değerleri sırasıyla %0,8 ve %0,56–1,15 idi. Belirlenen normal tiroid teknesyum-99m perteknetat alım aralığı %0,26–1,64 oldu. Yaş ve teknesyum-99m perteknetat alımı arasında negatif korelasyon gözlendi (r=-0,33; p=0,002).

Sonuç: Türkiye'de kullanımda olanlara kıyasla anlamlı biçimde daha düşük değerlere dayanan yeni normal tiroid teknesyum-99m perteknetat alım aralığımızın, İstanbul nüfusunda tiroid hastalıklarında tiroid fonksiyonu değerlendirmelerinde kullanılmaya uygun olduğu savındayız.

Anahtar Sözcükler: teknesyum-99m perteknetat; tiroid; tiroid sintigrafisi

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INTRODUCTION

The thyroid uptake of radioactive iodine provides a quantitative method for the evaluation of thyroid gland function, commonly used for the differentiation of hyperthyroidism from other causes of thyrotoxicosis and determination of therapeutic dose range in hyperthyroid patients (1). Thyroid uptake imaging (TUI) can be performed using different radiopharmaceuticals, and the use of iodine-131 (I-131) poses a serious risk due to high radiation doses to the thyroid gland (1-3 rad/mCi administered) based on its long half-life and β-particle emission (2). Although recommended by the Society of Nuclear Medicine for use in TUI in patients with thyrotoxicosis, I-131 is not used in routine thyroid imaging in Turkey. Iodine-123 (I-123) is another radiopharmaceutical effective in thyroid imaging, with a shorter half-life (13 hours), a gamma photon suitable for imaging using conventional scintillation cameras (159 keV), and no β-radiation. On the other hand, the availability of I-123 is reduced by its high cost and complex production process in cyclotron (3). Technetium-99m (^{99m}Tc) pertechnetate is also used for thyroid scintigraphy and uptake imaging. Associated with lower costs, higher availability, less procedure time, less radiation to the patient, and preferable energy (140 KeV), ^{99m}Tc-pertechnetate remains a commonly used radiopharmaceutical in the evaluation of thyroid function (1). In most cases, all data required for accurate diagnosis are provided by the use of 99mTc-pertechnetate uptake and imaging, although the thyroid does not organify 99mTc-pertechnetate. With such advantages, ^{99m}Tc-pertechnetate is the radiopharmaceutical preferred by most nuclear medicine clinics in Turkey in evaluations of the thyroid gland.

The normal reference range for thyroid uptake in euthyroid people may vary according to many factors, including iodine consumption, medication, hormonal changes, geographical region, and conditions such as gestation (4–6), and has indeed changed over the last two decades (7). Also, it has been suggested that it should be validated specifically for a given population (8,9). According to published data, the normal range for thyroid uptake of ^{99m}Tc-pertechnetate varies substantially depending on region (10,11). Recently, Ramos et al. (0.4–1.7%), Hamunyela et al. (0.15–1.69%), Macauley et al. (0.2–2.0%), and Wang et al. (0.82–3.52%) studied the normal range for thyroid uptake of ^{99m}Tc-pertechnetate for their own societies (11–14).

There is currently no globally established normal range for thyroid uptake of ^{99m}Tc-pertechnetate. Based on data reported previously in the literature, the lower and upper limits for the Turkish population could be accepted to be 0.24 to 0.7% and 2.9 to 4.0%, respectively (1,15–17). In an effort to contribute to the literature, the present study aimed to determine the normal range for thyroid uptake of ^{99m}Tc-pertechnetate in a population living in Istanbul.

MATERIALS AND METHODS

Sample selection

The retrospective study included 73 consecutive patients (54 females, 19 males) living in Istanbul, Turkey, between February 2016 and December 2019. All patients underwent thyroid scintigraphy using ^{99m}Tc-pertechnetate as a component of parathyroid scintigraphy for parathyroid adenoma localization. Thyroid scintigraphy and uptake imaging were performed for 15–25 minutes after the intravenous injection of ^{99m}Tc-pertechnetate. In all patients, the thyroid function test results were normal 1 year before and after the imaging, and no nodule was seen on thyroid ultrasonography. We excluded patients with a history of cardiac, renal or thyroid disease and use of any medicine or supplement which might affect thyroid function. We also excluded patients who had received iodinated contrast or radionuclide administration within 6 months of thyroid imaging and those who had received radioiodine treatment. For all patients, biochemical evaluation of thyroid function was performed in laboratory conditions. Patient characteristics are summarized in Table 1.

^{99m}Tc-pertechnetate scintigraphy

All ^{99m}Tc-pertechnetate uptake data were provided from two tertiary referral hospitals. Thyroid scintigraphy as a component of dual-tracer parathyroid subtraction scintigraphy was before the parathyroid scintigraphy, which was not within the scope of the present study. Each patient received 100 MBq of ^{99m}Tc-pertechnetate intravenously. The percentage uptake of ^{99m}Tc-pertechnetate by the thyroid gland was deter-

Figure 1. The %uptake distribution by age and sex

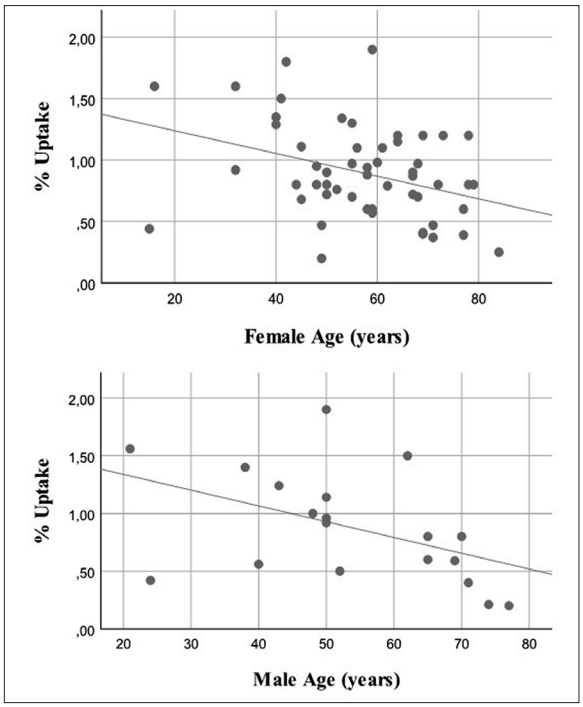
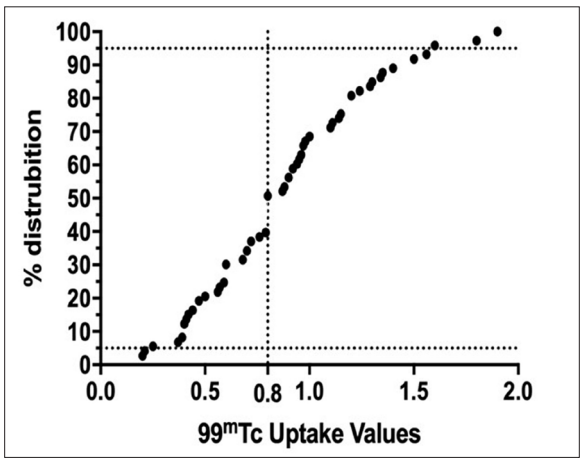


Figure 2. The cumulative %uptake line for all participants



The dotted lines represent the 5th and 95th percentiles.

mined at the 20th minute by using scintigraphic imaging techniques. The images were obtained with dual-head gamma cameras (Mediso, Hungary), equipped with a low-energy, high-resolution, parallel-hole collimator, on 128x128 matrix and at zoom 2. Images of the syringe were obtained before and after radiopharmaceutical injection. The images of the syringe and anterior neck were obtained for 1 minute and for 100.000 counts, respectively. Thyroid uptake of ^{99m}Tc-pertechnetate at the 20th minute was calculated by the formula: Thyroid uptake % = ([thyroid counts – background counts] / [pre-injection syringe counts – post-injection syringe counts]) x 100%.

Statistical analysis

Statistical analysis was performed using the SPSS (v. 25) (IBM Corp.) and Prism (v. 5.0) (Graph Pad Software, Inc.) software packages. Normality of the data was checked using the Shapiro–Wilk test and histogram graphs. Descriptive statistics were presented as mean (±standard deviation) or median (interquartile range: minimum–maximum) values. Intergroup comparisons were made using the Mann–Whitney U test. $p<0.05$ was considered statistically significant.

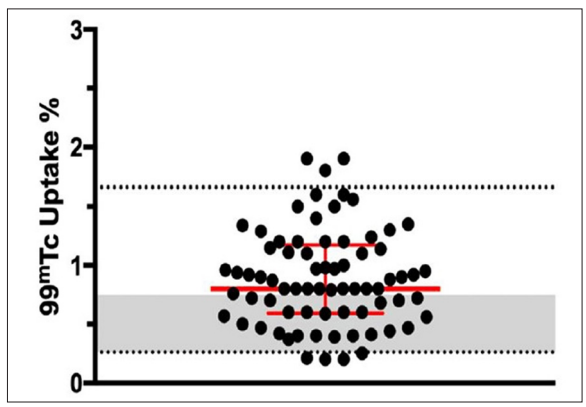
Study ethics

The study protocol was approved by the ethics committee of our hospital (2020-0166) and the requirement for obtaining informed consent was waived.

RESULTS

The study included a total of 73 patients, of whom 33 were from the Department of Nuclear Medicine, Faculty of Medicine, Istanbul Medeniyet University (Center 1), and 40 were from the Department of Nuclear Medicine, Haydarpaşa Numune Training and Research Hospital (Center 2). The mean patient age was 56.4±15.2 (range: 15–84) years, the mean thyroid-stimulating hormone (TSH) level was 1.15±0.48

Figure 3. The %uptake distribution for all participants



The dotted lines represent the 5th and 95th percentiles. The shadowed area highlights the values that would have been interpreted as low based on previous research.

Table 1. Center-based comparison of the mean values

	Center 1 (n=33)	Center 2 (n=40)	*p*
Age (years)	56.8±13.5	56.1±16.6	0.820
TSH (uIU/mL)	1.09±0.47	1.19±0.50	0.410
Free-T3 (pg/mL)	2.65±0.42	2.68±0.78	0.246
Free-T4 (ng/mL)	0.88±0.26	1.05±0.38	0.355
Uptake (%)	0.88±0.35	0.89±0.46	0.811

TSH: thyroid-stimulating hormone

Table 2. Sex comparison of the mean values

	Male (n=19)	Female (n=54)	*p*
Age (years)	53.8±15.6	58.0±14.1	0.413
TSH (uIU/mL)	1.31±0.66	1.45±0.90	0.979
Free-T3 (pg/mL)	2.65±0.66	2.70±0.39	0.933
Free-T4 (ng/mL)	1.05±0.44	0.93±0.26	0.223

TSH: thyroid-stimulating hormone

Table 3. Sex comparison of the median ^{99m}Tc-pertechnetate uptake values

	Median	Interquartile range	Observed range
Male (n=19)	0.80	0.54–1.24	0.2–1.90
Female (n=54)	0.80	0.57–1.14	0.2–1.90
All patients (N=73)	0.80	0.56–1.15	0.2–1.90

(0.35–2.05) uIU/mL, the mean free triiodothyronine (T3) level was 2.66±0.51 (0.94–3.34) pg/mL, and the mean free thyroxine (T4) level was 0.97±0.34 (0.01–2.83) ng/mL.

There was no statistically significant difference between the two center samples in terms of age, thyroid function test results, and uptake values (Table 1). Similarly, there was no significant difference between the two sexes in terms of age and thyroid function test results (Table 2). The median ^{99m}Tc-pertechnetate uptake values for both sexes and the entire population are presented in Table 3.

The percentage (%) uptake distributions by age for both sexes are presented in Figure 1. No significant correlation between age and %uptake was observed in either sex (for females, r=-0.128, p=0.368; for males, r=0.101, p=0.689). Thyroid uptake was found to be negatively correlated with age (r =-0.33, p=0.002) (Figure 1).

The thyroid uptake values were found to be non-normally distributed, and thus the reference range was represented by the range between the 5th and 95th percentiles: 0.26–1.64%. The cumulative %uptake line is shown in Figure 2, and the %uptake distribution is shown in Figure 3. Based on previous research, if the reference range had been accepted as 0.5–4%, 32.8% of the patient uptake results would have been interpreted as low (the shadowed area in Figure 3).

DISCUSSION AND CONCLUSION

In our study, the normal range for thyroid uptake of ^{99m}Tc-pertechnetate in a Turkish population of 73 was determined to be 0.26–1.64%. Both upper and lower limits of this range are significantly different from those in the normal range (0.5–4%) that is currently used in our tertiary referral hospitals and many other medical centers in Turkey (15). However, the currently used normal range (0.5–4%) may lead to underestimation in hyperthyroidism, which would result in a significant number of undiagnosed patients, who might suffer significant comorbidities such as arrhythmias, osteoporosis, and fractures. The range determined in our study is similar to those reported in recent studies from Brazil (0.4–1.7%), Namibia (0.15–1.69%), and the UK (0.2–2.0%), where lower values were not

considered anomalous (11–13). On the other hand, other studies conducted in China (0.82–3.52), the US (0.5–4.0%), and the UK (0.4–3.0%) reported ranges with higher limits than ours (14–16).

The very low uptake values in our study could be related to the dietary intake of iodine. Iodine consumption may affect the uptake of ^{99m}Tc-pertechnetate because iodide competes with ^{99m}Tc-99-pertechnetate for the transporter (18). Under the conditions of moderate iodine deficiency, the thyroid uptake of ^{99m}Tc-pertechnetate shows an inverse correlation with urinary iodine excretion as a substitute for iodine supply, but not with TSH (19). It has been reported that the reference range for ^{99m}Tc-pertechnetate uptake under TSH suppression will not change significantly when the iodine supply conditions turn from mild iodine deficiency to iodine sufficiency (20). Although variation in iodine intake is thought to be responsible for different thyroid uptake values, it is difficult to determine the exact relationship. As for our study, since it was not expected that our participants with a mean age of 59.4±14.4 years would be iodine-deficient, their iodine levels were not measured.

Another possible cause for lower thyroid uptake values is exposure to competitive inhibitors of the sodium iodide symporter, such as perchlorate, thiocyanate, and nitrate. Studies have shown that low iodine intake, coupled with concurrent exposure to such iodide uptake inhibitors, may result in decreased thyroid function (21–24). However, further research is needed to determine the possible role of these inhibitors in low ^{99m}Tc-pertechnetate uptake seen in a mildly iodine-deficient area.

Other important factors for different thyroid uptake measurements are intra- and inter-observer variations and different scintigraphy protocols, as has been reported recently (25). In our study, we compared values in patients from two tertiary hospitals and did not find any significant difference.

Similar to previous studies, we found a negative correlation between age and ^{99m}Tc-pertechnetate uptake (13,26). This could be explained by the physiological decline in iodine uptake secondary to a decrease in colloid content and follicular volume in elderly people (27). We think that age-related decrease in ^{99m}Tc-pertechnetate uptake should be considered while interpreting images of patients from different age groups. However, because of the small size of our sample, we did not perform an age-based analysis.

Finally, the present study has several limitations. In addition to the small sample size, we performed no urine iodine concentration evaluation to verify sufficient iodine intake. However, in Turkey the presence of iodine in table salt is regulated, and this is the reason why Istanbul is not an iodine-deficient area.

In conclusion, we propose that our new normal range for thyroid uptake of ^{99m}Tc-pertechnetate, based on significantly lower values compared with those currently in use in most hospitals in Turkey, is appropriate for use to evaluate thyroid function in thyroid disorders in the population of Istanbul. Our findings indicate that the normal reference ranges should be periodically revalidated for different regions and age groups in Turkey, which would require further prospective, larger-scale studies.

Conflict of Interest and Financial Disclosure

The author declares that he has no conflict of interest to disclose. The author also declares that he did not receive any financial support for the study.

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